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Wouters, Diederick B.; Bos, Rudolf R. M.; De Hosson, Jeff T.

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Will the hold of solid biodegradable implants be influenced by swelling during the degradation process?

An in-vitro study with Meniscus Arrows®

Diederick B. Wouters · Rudolf R. M. Bos · Jeff T. De Hosson

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Abstract Water uptake after implantation of biodegradable devices induces swelling, as mentioned in literature. The hold in bone of solid devices will increase if the swelling is substantial enough. The results of weighing six Meniscus Arrows® (MAs) before and after immersion in a sterile phosphate buffered saline solution during different time intervals were compared with the outcome of measurements under a field emission scanning electron microscope of six other MAs, stored under comparable conditions. The data were statistically evaluated with the Wilcoxon's signed rank test. The weight increase of 2.1 mg or 9.16% was statistically significant in the first 2 h following immersion, remaining stable afterwards with an average weight gain of 1.7 mg or 7.18%. The core diameter of the MAs increased to 0.01 mm or 1.01% with time. Although this is statistically significant, it is not expected to have any consequences for the hold. However, a remarkable and statistically significant decrease in the outer inter-barb diameter of 0.15 mm or 8.6% was noted with time. Mechanical testing should reveal the clinical relevance of the results of this study.

D. B. Wouters (✉)
Department of General and Arthroscopic Surgery and Traumatology, TweeSteden Hospital, Dr. Deelenlaan 5, 5042 AD, Tilburg, The Netherlands
e-mail: dwouters@tsz.nl

D. B. Wouters · R. R. M. Bos
Department of Oral and Maxillofacial Surgery, University Medical Centre, Hanzeplein 1, 9713 GZ, Groningen, The Netherlands

J. T. De Hosson
Department of Applied Physics, University of Groningen, Nijenborgh 4, 9747 AG, Groningen, The Netherlands

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Introduction

Three biodegradable polymers, i.e., polydioxanon, polyglycolic acid and polylactic acid, and their co-polymers, combinations or blends, are currently used for the production of biodegradable devices to fix fracture fragments in humans. In the optimal situation, their mechanical properties allow consolidation of the bony fragments that they fix and their resorption passes off without negative side effects [1].

Degradation occurs mainly by the uptake of water during the hydrolization process and to a lesser extent by enzymatic influence [2–4]. Several factors affect this degradation; one is the increase of specific surface and the other is hydrophilia, both promoting the uptake of water. Further, amorphous regions are more susceptible to the hydrolytic attack of the chemical bonds than crystalline regions. In this way, the long polymeric chains are cut into shorter chains by the water molecules that act as molecular scissors. These short chains slip easier passing each other, leading to a decrease in polymer strength and to fragmentation of the material. This enhances the susceptibility to further degradation [5, 6]. The small fragments are phagocytized by macrophages during the physiological inflammatory response [6–8]. The circumstances at the implantation site effect the resorption process as well [9, 10].

The uptake of water during this degradation process induces a swelling or distention of the polymeric material [4, 7, 8]. If this is substantial, the initial fixation of the devices in bone could be enhanced. Thus this phenomenon could influence the mechanical properties in view of the clinical application.

Table 1 Change in weight of six Meniscus Arrows® during 28 days of immersion

Arrow no.	Thrs = 0 (t_1)	Thrs = 2 (t_2)	Thrs = 4 (t_3)	Thrs = 6 (t_4)	Thrs = 8 (t_5)
1	0.0228	0.0254	0.0244	0.0240	0.0241
2	0.0226	0.0246	0.0247	0.0245	0.0241
3	0.0226	0.0248	0.0244	0.0244	0.0245
4	0.0226	0.0246	0.0245	0.0243	0.0246
5	0.0228	0.0245	0.0241	0.0246	0.0244
6	0.0230	0.0250	0.0243	0.0250	0.0246
Weight increase[a] (%)		9.16	7.34	7.62	7.26
Arrow no.	Thrs = 24 (t_6)	Thrs = 28 (t_7)	Thrs = 32 (t_8)	Thrs = 48 (t_9)	Thrs = 60 (t_{10})
1	0.0250	0.0251	0.0242	0.0242	0.0240
2	0.0260	0.0240	0.0243	0.0241	0.0243
3	0.0246	0.0244	0.0243	0.0244	0.0249
4	0.0241	0.0242	0.0243	0.0252	0.0245
5	0.0244	0.0244	0.0247	0.0253	0.0256
6	0.0246	0.0249	0.0245	0.0250	0.0245
Weight increase[a] (%)	9.03	7.77	7.26	8.65	8.36
Arrow no.	Td = 3 (t_{11})	Td = 4 (t_{12})	Td = 8 (t_{13})	Td = 10 (t_{14})	Td = 14 (t_{15})
1	0.0248	0.0238	0.0249	0.0246	0.0243
2	0.0251	0.0247	0.0248	0.0242	0.0241
3	0.0247	0,0246	0.0249	0.0243	0.0248
4	0.0242	0,0248	0.0246	0.0245	0.0250
5	0.0248	0.0254	0.0256	0.0249	0.0254
6	0.0242	0.0250	0.0244	0.0243	0.0244
Weight increase[a] (%)	8.37	8.28	9.39	7.63	8.51
Arrow no.	Td = 18 (t_{16})	Td = 28 (t_{17})			
1	0.0244	0.0244			
2	0.0246	0.0240			
3	0.0245	0.0242			
4	0.0241	0.0241			
5	0.0242	0.0248			
6	0.0241	0.0247			
Weight increase[a] (%)	6.97	7.18			

Thrs time in hours after $t = 0$, *Td* = time in days after $t = 0$

[a] Average increase in weight compared to the weight at $t = 0$

In general, this swelling or distention, due to the uptake of water, has been related to an increase in weight of the material [11–15]. In fact, only a few authors measure the increase of the dimensions in some way and term this swelling [4, 16, 17].

In this study, the change in the weight of six Meniscus Arrows® made of 96L-4D PLA (PLA96) over time is compared to the change in the size of the devices by measuring their dimensions under a field emission scanning electron microscope.

Methods

Six Meniscus Arrows® (MAs, Bionix Implants Ltd., Tampere, Finland), were weighed by means of a balance (Satorius) with an accuracy of 0.1 mg. Subsequently, they were submerged in a sterile phosphate buffered saline solution (PBS, Pharmacy of the University Medical Centre, Groningen, The Netherlands) at 37°C. Reweighing was performed after drying the MAs with tissue paper at 2, 4, 6, 8, 24, 28, 32, 48, 60 h and 7, 10, 14, 18, 28 days later.

Parallel to this series, the core diameter and the distance between the tips of the barbs of a second series of 6 MAs were measured (Figs. 2, 5) with a field emission scanning electron microscope (type Philips FEG XL-30), also starting at $t = 0$ (t_1) and at 2, 4, 6 and 24 h and 3, 4, 5, 7, 11 and 18 days afterwards. The data were rounded off at an accuracy of 10 μm (Figs. 2, 5). In between these measurements, the MAs were kept submerged in the PBS solution at 37°C as well. This experiment was finished after 18 days, achieving, statistically, sufficient results. All the results were statistically evaluated with the Wilcoxon's signed rank test.

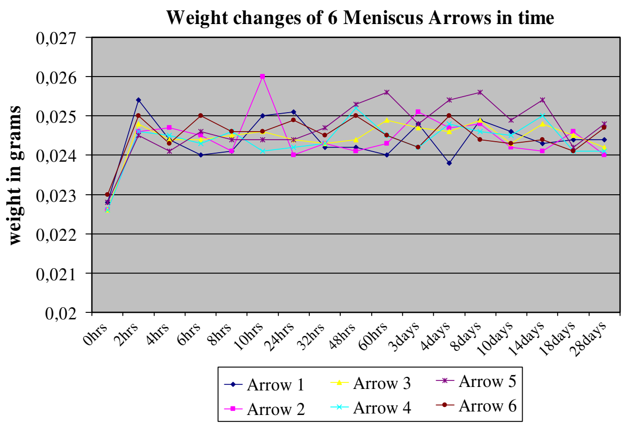

Fig. 1 The change in weight of six Meniscus Arrows® during 28 days of immersion

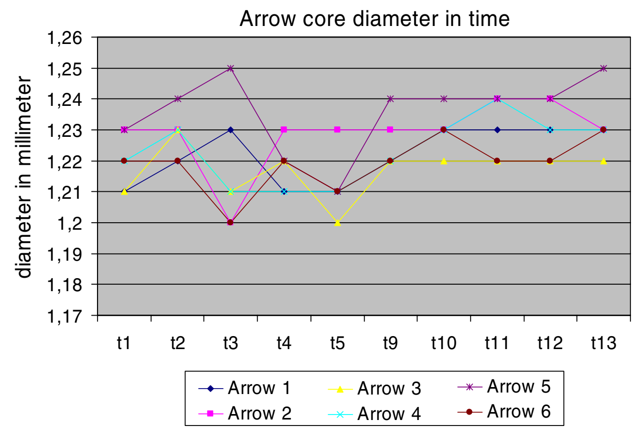

Fig. 3 The change in the core diameter of six Meniscus Arrows® during 18 days of immersion

Results of the weight experiment (Table 1, Fig. 1)

The weight of the MAs increased during the first 2 h from an average of 0.0227 g (SD = 0.000163) to an average of 0.0248 g (SD = 0.000337) or 9.16%. This is significant ($P = 0.027$). After 2 h the weight remained stable at an average weight gain of 0.0017 g or 7.18% after 28 days ($t = 17$). The average weight varied in this period from 0.024 to 0.025 g. This variation is not significant (Table 1, Fig. 1).

Results of the swelling experiment (Figs. 2, 3, 4, 5; Table 2)

A subtle increase in the core diameter of the arrows over time was noted. The average diameter increased by 0.01 mm, or 1.01%, from 1.22 mm (standard deviation (SD) = 0.0089) at $t_1 = 0$ to 1.23 mm at t_{13} (t_1 + 18 days) (SD = 0.0098). This is significant ($P = 0.031$) (Table 2, Figs. 2, 3, 4, 5).

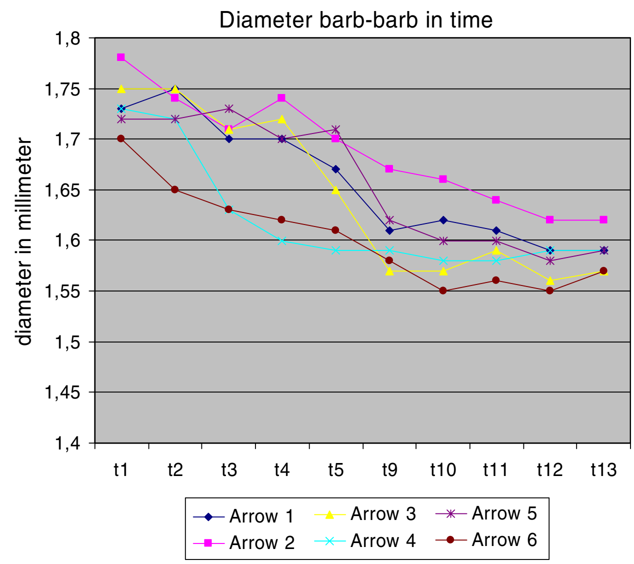

Fig. 4 The change in the barb–barb diameter of six Meniscus Arrows® during 18 days of immersion

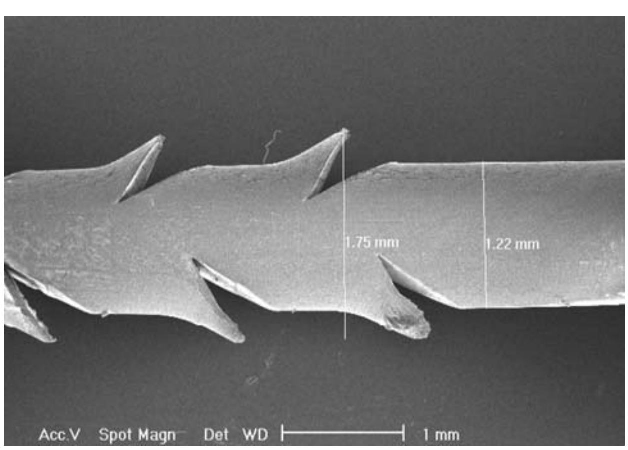

Fig. 2 Example of the shape and measurement of arrow 1 at t_2 or 2 h after the start of the experiment and after being submerged for 2 h

The barb–barb diameter decreased significantly ($P = 0.031$) over time by 0.15 mm, or 8.6%, from an average of 1.74 mm at t_1, (SD = 0.0274) to 1.59 mm (SD = 0.01897) at t_{13} (Table 2).

Discussion

The application of biodegradable osteofixation devices could have several advantages over metallic implants. Mechanical factors like erosion of the opposite cartilage, if inserted in a joint surface, and stress shielding [18–22] as well as scatter in computed tomography and magnetic

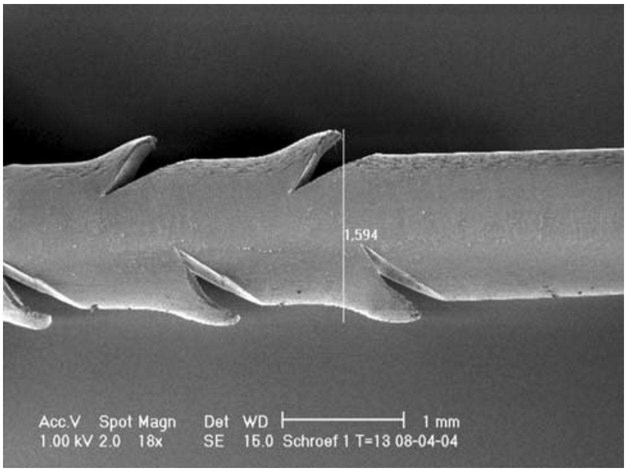

Fig. 5 Example of the change in shape and measurement at t_{13}: arrow 1, 18 days after the start of the experiment

resonance imaging [23, 24], and the possibility of evoking allergic and carcinogenic reactions [25] induced the need of a subsequent removal operation of the metallic devices in most circumstances. This second operation could be avoided, using biodegradable rods, pins, plates or screws [1, 8, 18–22, 26].

Distention could be another advantage of intra-osseous placed biodegradable osteofixation implants, leading, theoretically, like the mechanism of expanding bolts in a solid material, to an increased fixation in the bone.

MAs, designed for repairing meniscus tears, could potentially be used to fix the cartilage–bone fragments in the treatment of osteochondritis dissecans disease [26] or other small bony fragments in fracture surgery. If they distend substantially, the pull-out force and fixation in the bone would considerably increase.

In literature, swelling of biodegradable polymers is mostly related to an increase in weight. On the contrary, the mechanical distention has been scarcely measured [5, 12–15]. In two papers, the increase in volume and the macroscopic measurement of the dimension along a ruler was defined as swelling [11, 16], in one, without giving the exact data of the distention [11]. In another paper, the dimensional change in vitro was measured and determined, as was the weight [17]. These last three papers described hydrogels. Finally, Hasirci measured in his study the change in the size of rods of reinforced poly (lactide-co-glycolide) during the in vitro part of the experiment [4]. However, the experimental procedure itself is not fully transparent to us.

In the present study, the change in weight of the 6 MAs were measured during 28 days (Table 1, Fig. 1). This period is the expected initial consolidation time for fractures with small fragments in humans.

In the first 2 h, the weight increased rapidly and significantly by 9.16%, remaining stable afterwards at 7.18% weight gain. The core diameter, however, increased gradually and slightly (0.01 mm or 1.01%), but significantly, during the whole period. This reveals an evident discrepancy in this experiment between the increase in the weight and the dimensions.

In contrast, in literature much higher swelling (or weight gain) ratios are mentioned of different polymers, e.g., more than 30% of a cross-linked poly (propylene fumarate) PLA/PGA 70/30 complex at 28 days [4], 260% at 12 h of a phosphate containing polyethylene glycol methacrylate

Table 2 Change in core diameter and barb–barb diameter of six Meniscus Arrows® during 18 days of immersion

Core diameter										
	T = 1	*T* = 2	*T* = 3	*T* = 4	*T* = 5	*T* = 9	*T* = 10	*T* = 11	*T* = 12	*T* = 13
Arrow 1	1.21	1.22	1.23	1.21	1.21	1.22	1.23	1.23	1.23	1.23
Arrow 2	1.23	1.23	1.2	1.23	1.23	1.23	1.23	1.24	1.24	1.23
Arrow 3	1.21	1.23	1.21	1.22	1.2	1.22	1.22	1.22	1.22	1.22
Arrow 4	1.22	1.23	1.19	1.19	1.2	1.22	1.23	1.24	1.23	1.23
Arrow 5	1.23	1.24	1.25	1.22	1.21	1.24	1.24	1.24	1.24	1.25
Arrow 6	1.22	1.22	1.17	1.22	1.21	1.22	1.23	1.22	1.22	1.23
Average	1.22	1.23	1.21	1.22	1.21	1.23	1.23	1.23	1.23	1.23
Barb–barb diameter										
Arrow 1	1.73	1.75	1.7	1.7	1.67	1.61	1.62	1.61	1.59	1.59
Arrow 2	1.78	1.74	1.71	1.74	1.7	1.67	1.66	1.64	1.62	1.62
Arrow 3	1.75	1.75	1.71	1.72	1.65	1.57	1.57	1.59	1.56	1.57
Arrow 4	1.73	1.72	1.63	1.6	1.59	1.59	1.58	1.58	1.59	1.59
Arrow 5	1.72	1.72	1.73	1.7	1.71	1.62	1.6	1.6	1.58	1.59
Arrow 6	1.7	1.65	1.63	1.62	1.61	1.58	1.55	1.56	1.55	1.57
Average	1.74	1.72	1.67	1.68	1.66	1.61	1.60	1.60	1.58	1.59

polymer [16] and 310% at 12 weeks for oligo (poly(ethylene glycol) fumarate) [17]. The origin of this discrepancy between our results and the data from literature is not clear. Is it only related to this specific DLPLA complex, to the measure method as well, or other influences?

We assume, however, that the 0.01 mm or 1.01% increase in the core diameter in 18 days will not have any impact on the mechanical performance in 28 days, because the increase is minimal and very gradual (Fig. 3). Furthermore, taking the trend of the data into account, it is not to be expected that this pattern will alter in 10 more days and, in vivo, the progressive consolidation of the fixed fragments will decrease the demands on the mechanical performance of the fixation.

In contrast, the inter-barb diameter decreased steadily in 18 days by 0.15 mm, or 8.6%, caused by a curling of the barbs (Figs. 2, 4, 5). Hypothetically, this can be explained by a tendency of the material to return to its original rod-like shape during degradation, i.e., a state before the barbs were created. These barbs are fabricated by cutting a rod of PLLA during the plastic deformable phase of the raw material, followed by bending the cut material externally (Fig. 2). Theoretically, this decrease in the outer diameter and shape would imply that the hold of biodegradable devices like MAs will not increase like expanding bolts as a function of time, but on the contrary decrease. Nevertheless, it is limited to less than 10% in 18 days and since the consolidation process of the fragments in the clinical situation will continue over time, the mechanical demands on the fixation of the fragments will decrease. These effects can neutralize each other and therefore the clinical impact is not obvious.

Conclusion

The swelling of solid biodegradable polymers, as often mentioned in literature, judging from the results of our study, is more related to an increase in weight by the uptake of water than to a swelling or distention of the devices.

Therefore, the hold in bone of these biodegradable polymers will not increase like the increased fixation of an expanding bolt in a solid material. Theoretically, the tendency of the material to retract into its original shape, as found in our experiment, could influence the fixation capacities in a negative sense. However, the clinical importance of this phenomenon is not clear, as the fragment will gain stability progressively, due to the ongoing consolidation process. Besides, the absolute values found in our tests are relatively small.

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References

1. Bos RRM (1989) Poly(L-lactide) osteosynthesis: development of bioresorbable bone plates and screws. Thesis, University of Groningen, pp 7–9
2. Williams DF, Mort E (1977) Enzyme-accelerated hydrolysis of polyglycolic acid. J Bioeng 1:231– 238
3. Williams DF (1979) Some observations on the role of cellular enzymes in the in-vivo degradation of polymers. Spec Tech Publ 684:61–75
4. Hasirci V, Lewandrowski K, Gresser JD, Wise DL, Trantolo DJ (2001) Versatility of biodegradable biopolymers: degradability and an in vivo application. J Biotechnol 86(2):135–150
5. Yoon JJ, Park TG (2001) Degradation behaviors of biodegradable macroporous scaffolds prepared by gas foaming of effervescent salts. J Biomed Mater Res 55(3):401–408
6. Pietrzak WS, Sarver DR, Verstynen ML (1997) Bioabsorbable polymer science for the practicing surgeon. J Craniofac Surg 8(2):87–91
7. Pego AP, Van Luyn MJ, Brouwer LA, van Wachem PB, Poot AA, Grijpma DW, Feijen J (2003) In vivo behavior of poly(1,3-trimethylene carbonate) and copolymers of 1,3-trimethylene carbonate with D, L-lactide or epsilon-caprolactone: degradation and tissue response. J Biomed Mater Res 67A(3):1044–1054
8. Bergsma EJ, de Bruijn WC, Rozema FR, Bos RRM, Boering G (1995) Late degradation tissue response to poly(L-lactide) bone plates and screws. Biomaterials 16(1):25–32
9. Tschakaloff A, Losken HW, von Oepen R (1994) Degradation kinetics of biodegradable D, L-polylactid acid biodegradable implants depending on the site of implantation. Int J Oral Maxillofac Surg 23:443–445
10. Sevastjanova NA, Mansurova LA, Dombrovskova LE, Slutskii LI (1987) Biochemical characterisation of connective tissue reaction to synthetic polymer implants. Biomaterials 8:242–247
11. Wang Y, Kim YM, Langer R (2003) In vivo degradation characteristics of poly(glycerol sebacate). J Biomed Mater Res 66A(1):192–197
12. Dijkhuizen-Radersma van R, Roosma JR, Kaim P, Métairie S, Péters FLAMA, Wijn de J, Zijlstra PG, Groot de K, Bezemer JM (2003) Biodegradable poly(ether–esther) multiblock copolymers for controlled release applications. J Biomed Mater Res 67A:1294–1304
13. Yang Z, Zhang Y, Markland P, Yang VC (2002) Poly(glutamic acid) poly(ethylene glycol) hydrogels prepared by photoinduced polymerization: synthesis, characterization, and preliminary release studies of protein drugs. J Biomed Mater Res 62(1):14–21
14. Bezemer JM, Oude Weme P, Grijpma DW, Dijkstra PJ, van Blitterswijk CA, Feijen J (2000) Amphiphilic poly(ether ester amide) multiblock copolymers as biodegradable matrices for the controlled release of proteins. J Biomed Mater Res 52(1):8–17
15. Tanahashi K, Jo S, Mikos AG (2002) Synthesis and characterization of biodegradable cationic poly(propylene fumarate-co-ethylene glycol) copolymer hydrogels modified with agma tine for enhanced cell adhesion. Biomacromolecules 3(5):1030–1037

16. Wang DA, Williams CG, Li Q, Sharma B, Elisseeff JH (2003) Synthesis and characterization of a novel degradable phosphate-containing hydrogel. Biomaterials 24(22):3969–3980
17. Shin H, Quinten Ruhe P, Mikos AG, Jansen JA (2003) In vivo bone and soft tissue response to injectable, biodegradable oligo(poly(ethylene glycol) fumarate hydrogels. Biomaterials 24(19):3201–3211
18. Cugat R, Garcia M, Cusco X, Monllau JC, Vilaro J, Juan X, Ruiz-Cotorro A (1993) Osteochondritis dissecans: a historical review and its treatment with cannulated screws. Arthroscopy 9(6):675–684
19. Wagner H (1976) Die Kliniek der Knorpeltransplantation bei der Osteochondrosis dissecans. Hefte zur Unfallheilkunde 127:118–125
20. Gschwend N, Munzinger U, Löhr J (1981) Unsere extraarticuläre Dissecatverschraubung bei Osteochondrosis dissecans des Kniegelenkes. Orthopäde 10:83–86
21. Johnson LL, Uitvlugt G, Austin MD, Detrisac DA, Johnson CJ (1990) Osteochondritis dissecans of the knee: arthroscopic compression screw fixation. Arthroscopy 6(3):179–189
22. Kivistö R, Pasanen L, Leppilahti J, Jalovaara P (2002) Arthroscopic repair of osteochondritis dissecans of the femoral condyles with metal staple fixation: a report of 28 cases. Knee Surg Sports traumatol Arthrosc 10:305–309
23. Scher N, Poe D, Kuchmir F, Reft C, Weichselbaum R, Panje WR. (1988) Radiotherapy of the resected mandible following stainless steel plate fixation. Laryngoscope 98:561–563
24. Castillo MH, Button TM, Homs MI, Pruett CW, Doerr R (1988) Effects of radiation therapy on mandibular reconstruction plates. In: Trans 41st annual cancer symposium, The Society of Surgical Oncology, New Orleans, p 144
25. Black J (1988) Orthopedic biomaterials in research and practice. Churchill Livingstone, New York, Edinburgh, London, Melbourne, pp 292–302
26. Wouters DB, Bos RRM, Mouton LJ, van Horn JR (2004) The Meniscus Arrow® or metal screw for treatment of Osteochondritis dissecans? In vitro comparison of their effectiveness. Knee Surg Sports Traumatol Arthrosc 12:52–57